AHCC®

Clinical Overview

Use

The medical literature documents the use of AHCC (active hexose correlated compound) as an immunomodulatory agent, as well as efficacy as an adjuvant in cancer treatment and various infections. Clinical trials have also examined the use of AHCC in the treatment of inflammatory bowel disease (IBD) and as a hepatoprotective agent. However, clinical data are lacking to recommend AHCC for any of these indications.

Dosing

AHCC is primarily available as a capsule. Manufacturer dosing guidelines recommend two 500 mg capsules orally 3 times a day on an empty stomach, or 2 capsules orally daily for general well-being. Dosages up to 6 g/day have been used.

Contraindications

Avoid use in individuals hypersensitive to any of the components of AHCC or to basidiomycete mushrooms.

Pregnancy/Lactation

Information regarding safety and efficacy in pregnancy and lactation is lacking.

Interactions

Use with caution in patients taking aromatase inhibitors and medications metabolized via cytochrome P450 (CYP-450) 2D6.

Adverse Reactions

A phase 1 trial reported mild GI complaints, including nausea, diarrhea, and bloating. Some patients also reported headache, fatigue, and foot cramps with the liquid form of AHCC. AHCC is generally well tolerated.

Toxicology

In a phase 1 trial, AHCC 9 g/day for 14 days had minimal adverse effects and was well tolerated by most patients.

Source

AHCC is an extract prepared from mycelia of several species of basidiomycete mushrooms, including shiitake or Lentinula edodes, after being cultured in a liquid medium. Kenner 2001, Kidd 2000

History

AHCC was developed in 1987 at the University of Tokyo Faculty of Pharmaceutical Sciences, along with other researchers, as a natural product for use in regulating high blood pressure. However, AHCC is now primarily known for its immunostimulant potential in protecting against viruses, cancers, and infections. Kenner 2001, Kidd 2000 AHCC is being researched in the United States, China, Korea, Japan, and Thailand. Its use as a nutritional supplement is most common in Japan and the United States. Belay 2015 AHCC has been used as a supplement for patients with cancer, HIV/AIDS, hepatitis C, hypertension, and autoimmune diseases. There are also anecdotal claims of use in treating wounds, stomach ulcers, gum disease, fatigue syndrome, parasites, and multiple sclerosis. Kenner 2001, Pescatore 2008

Uses and Pharmacology

The medical literature documents the use of AHCC as an immunomodulatory agent, as well as efficacy as an adjuvant in cancer treatment and various infections.

Cancer

AHCC is thought to modulate tumor immune surveillance by regulating innate and adaptive immune system responses. The compound may act as a biological response modifier by enhancing natural killer cell activity, interleukin 12 (IL-12) and tumor immunity production, and spleen cell proliferation and cytokine production. Gao 2006

In vitro and animal data

In an in vitro and helped to reduce metastasis of rat mammary adenocarcinoma. Matsushita study, the combination of AHCC plus UFT (tegafur and uracil in a 4:1 molar concentration) enhanced natural killer cell activity in tumor-bearing rats, while UFT treatment alone depressed the natural killer cell activity. The combination also enhanced nitric oxide production and cytotoxicity of peritoneal macrophages. In addition, AHCC restored suppressed mRNA expression of IL-1alpha and tumor necrosis factor (TNF)-alpha induced by the chemotherapy 1998

In a study in rats, AHCC partially suppressed DNA fragmentation on thymus apoptosis induced by dexamethasone. AHCC may act as an antioxidant to suppress thymic apoptosis or may stimulate the melatonin secretion that protects thymocytes. Burikhanov 2000 AHCC administration enhanced the serum levels of IL-12, a critical cytokine for immune system responses in anticancer therapy, in H-2b mice and was effective in genetically Th1 (or transcription factor T-bet)–dominant mice.Yagita 2002

AHCC may help protect against adverse reactions caused by anticancer drugs. The compound protected against alopecia in rats treated with cytosine arabinoside. Liver injury was reduced when rats treated with mercaptopurine and methotrexate were simultaneously given with AHCC AHCC at a dose of 1 g/kg.Sun 1999

Cisplatin-induced antitumor activity was enhanced treatment in a study of mice. AHCC supplementation improved the suppression of bone marrow caused by cisplatin, and histopathological examination of the kidney revealed a renal protective effect. Hirose 2007

In vitro treatment of gemcitabine-resistant pancreatic cancer KLM1-R cells, but not high-mobility group box 1 (HMGB1) cells, with AHCC 10 mg/mL for 48 hours decreased protein expression of heat shock factor 1 (HSF1), which suggests that HSF1 is downregulated by AHCC.

AHCC shows promise as a potential component of anticancer drug regimens for drug-resistant cancer cells. Tokunaga 2015

In vitro treatment of gemcitabine-resistant pancreatic cancer KLM1-R cells with AHCC 10 mg/mL reduced protein expression of the Sex-determining region Y-box 2 (SOX2). Protein expression was not reduced in Oct4 or Nanog, which suggests that AHCC targets the downregulation of SOX2. Given these findings, AHCC may have the potential to enhance the effect(s) of chemotherapy while reducing its adverse effects, particularly in pancreatic cancer. Nawata 2014

In another study, gemcitabine-resistant pancreatic cancer KLM1-R cells were treated with 0, 1, 5, and 10 mg/mL of AHCC for 48 hours. Protein expression of HSP27 was reduced with AHCC treatment; results differed based on dose, indicating a dose-dependent relationship between HSP27 protein levels and AHCC. AHCC also had a cytotoxic effect on KLM1-R cells that was higher when AHCC was combined with gemcitabine. These results indicate that AHCC downregulates expression of HSP27 and that combined treatment with gemcitabine synergistically increases the cytotoxic effect. Suenaga 2014

One study evaluated the activity of AHCC (50 mg/kg orally once daily for 12 weeks) alone or in combination with tamoxifen or letrozole in 2 mouse models of estrogen receptor–positive breast cancer: catechol-*O*-methyltransferase (COMT) (MCF-7 variant) and COMT wild-type (ZR-75 variant). The MCF-7 model showed a significant decrease in tumor growth with AHCC alone and in combination with tamoxifen. The MCF-7 model also showed a decrease in letrozole aromatase inhibitor efficacy when given in combination with AHCC, which may be due to AHCC induction of aromatase activity that decreases detoxification of oncogenic catechol estrogens. The ZR-75 model showed a decrease in tumor growth with AHCC alone and in combination with letrozole.Mathew 2017

Both in vitro and in mice (at a dosage of 600 mg/kg given by gavage twice per week for 2 weeks), AHCC increased Caspase-3–dependent apoptosis of acute myeloid leukemia (AML) cells, as well as induced Fas and Caspase-8, both members of the extrinsic apoptotic pathway. This led to reduced blast counts and increased survival time in mice. With increasing doses of AHCC, there were significantly fewer colonies. Results demonstrate that AHCC has a direct effect on AML blasts, reducing viability and proliferation in AML cell lines and primary AML samples. AHCC also decreased white blood cell counts. AHCC can cause AML cell death in both MV4-11 cells as well as in primary AML samples. Fatehchand 2017

AHCC 100 mcL (100 mg/mL concentration) dissolved in deionized distilled water was given orally to mice for 2 weeks in combination with 100 mcL (200 mcg/mL concentration) of KSK-CpG ODN, an immunological adjuvant, via intraperitoneal injection twice a week. There was a reduction in tumor size in the B16 melanoma murine model in the treatment groups. Treatment groups also displayed lower total white blood cell counts, increased production of nitric oxide, increased protein concentration of IL-10, and lower reactive oxygen species production compared to the control group.Ignacio 2015

Clinical data

In patients with malignant tumors, AHCC may increase circulating levels of TNF, interferon (IFN)-gamma, and IL-1B.Burikhanov 2000 In a 2-week study, 3 and 6 g/day of AHCC increased natural killer cell activity in 3 patients with different types of advanced cancer: rhabdomyosarcoma, multiple myeloma, and breast cancer.Ghoneum 1992 The binding capacity of natural killer cells to tumor cells was enhanced 2-fold in 17 cancer patients with different advanced malignancies treated with 3 g/day of AHCC orally for 2 to 6 months.Ghoneum 1994 A similar 2-week study also documented a decline of tumor-associated antigens in 8 of 11 patients treated with AHCC. The mechanism of action was associated with enhanced natural killer cell activity due to an increase of natural killer cell granularity and binding capacity to tumor cell targets.Ghoneum 1995 Compared with baseline, IL-12, IFN-gamma, and natural killer cell activity all increased to normal levels after treatment with AHCC in a study of 38 patients with solid tumors.Katsuaki 2000

AHCC may improve the prognosis in postoperative advanced liver cancer patients by reducing incidences of recurrence or death due to hepatocellular carcinoma or liver cirrhosis.Cowawintaweewat 2006, Matsui 2002

Serologic response improved after treatment with AHCC in a 66-year-old patient with castration-resistant prostate cancer, an incurable condition with limited treatment options.Turner 2009

One study of 12 patients with different cancers reported that AHCC can be used to help prevent bone marrow depression resulting from chemotherapy.Won 2002

In one study, female patients receiving adjuvant chemotherapy for breast cancer were given 1 g of AHCC orally after each meal to determine its effects on the adverse events associated with chemotherapy. Patients were also given dexamethasone and 5-hydroxytriptamine 3 (5-HT_3) receptor antagonists to prevent nausea and vomiting. The AHCC group experienced fewer adverse neutrophil events compared with the control group. The AHCC group also required less granulocyte colony-stimulating factor during taxane therapy. These results indicate that AHCC improves bone marrow suppression, although the mechanism is unclear. AHCC has the potential to increase neutrophil count during bone marrow suppression, indicating it may be possible to increase the intensity of chemotherapy sessions, potentially resulting in better clinical outcomes. This study also showed that AHCC 1 g orally administered after each meal may improve lipid abnormalities in breast cancer patients undergoing chemotherapy.Hangai 2013

In a study of patients with unresectable pancreas ductal adenocarcinoma, AHCC 6 g was given daily for 8 weeks along with 2 cycles of gemcitabine to assess the clinical effects of AHCC on adverse events caused by gemcitabine. Compared with the control group, patients receiving AHCC demonstrated higher hemoglobin and serum albumin levels, lower C-reactive protein (CRP) levels, and less frequent occurrence of taste disorder. The pre-post ratio of albumin was higher with AHCC, while that of CRP was lower than in the control group. The AHCC group showed better modified Glasgow Prognostic Scores (mGPS) as well as a lower frequency of grade 3 in mGPS. Response Evaluation Criteria in Solid Tumor (RECIST) response rates and disease control rates were better in the AHCC group. The AHCC group also demonstrated a longer median survival time and higher overall tendency for survival. These results suggest that AHCC may improve gemcitabine-induced adverse events in pancreas ductal adenocarcinoma patients.Yanagimoto 2016

In a study evaluating the safety and efficacy of AHCC on chemotherapy-induced adverse effects and quality of life, advanced cancer patients were given of AHCC 3 g/day orally during a course of chemotherapy. Specifically, hepatotoxicity, hematotoxicity, and DNA levels of human herpesvirus type 6 (HHV-6; a possible biomarker of fatigue during chemotherapy) were evaluated. Results showed that in female patients, quality of life was increased and symptoms of appetite loss were improved. In all patients, AHCC reduced symptoms of fatigue. Scores for dyspnea increased after chemotherapy with AHCC supplementation. The antioxidant actions of AHCC have been determined to be moderate.Ito 2014

In a study evaluating the effects of AHCC on immune response and adverse events in epithelial ovarian cancer or peritoneal cancer patients taking platinum-based chemotherapy, patients were given two 500 mg AHCC capsules orally 3 times a day throughout 6 cycles of chemotherapy. Changes in $CD4^+$ and $CD8^+$ T-cell lymphocytes were not significantly different between the AHCC and placebo groups; however, $CD8^+$ levels were significantly higher in the AHCC group at the sixth cycle of chemotherapy. Nausea and vomiting associated with chemotherapy decreased in the AHCC group.Suknikhom 2017

Head and neck cancer patients were given 3 g of dried AHCC extract every morning 3 days prior to chemotherapy. The extract was well tolerated, with most patients reporting they felt better and stronger at the time of chemotherapy cycle initiation. Patients' sleep patterns were more regulated, visitor interactions increased, and appetites improved. Furthermore, a reduction in the rate of decrease in hemoglobin was observed, no patients required concentrate transfusion, and the majority of patients saw a decrease in GI-related chemotherapy adverse effects with AHCC.Parida 2011

Immunomodulatory effects

In vitro and animal data

In a cold-induced stress mouse model for investigating effects of AHCC on Chlamydia trachomatis genital infection and immune response, mice were given AHCC 300 mg/kg orally for 31 days. An improvement in body weight gain and spleen weight gain was observed in AHCC-fed stressed mice. On day 3, the AHCC-fed mice also showed a lower intensity of C. trachomatis infection, which was further evidenced by reduced shedding from the genital tract on day 18. Levels of cytokines were also measured in vitro. There were increases in TNF-alpha and IL-6 by peritoneal cells and increases in IL-2 and IFN-gamma production in splenic T cells in AHCC-fed mice. These results suggest that AHCC may restore cytokine production in stressed environments. The increase in cytokines may account for the fact that decreased C. trachomatis shedding was observed. Overall, these results suggest that AHCC restores immune system functions.Belay 2015

Clinical data

In a placebo-controlled study of healthy individuals, an AHCC dose of 4 capsules (250 mg/capsule) was taken daily for 4 weeks to evaluate its effects on seasonal suppression of immune competence. Results showed immunomodulatory effects against seasonal changes in those taking AHCC during the winter months. There was an insignificant decrease in the number of natural killer cells in the AHCC group compared to placebo, which suggests AHCC maintains the natural killer cell count during the winter months, during which natural killer cell count normally drops (as indicated by the placebo group). Subjects taking AHCC showed greater increase in natural killer cell activity compared with the placebo group. Furthermore, the AHCC group did not demonstrate altered immune competence, as measured by the score of immunological vigor, which suggests that AHCC maintains total immunity against immune suppression caused by seasonal changes. AHCC also showed promise in maintaining neutrophil and lymphocyte homeostasis, with no changes in neutrophil or lymphocyte counts observed. AHCC also showed improvement in mood compared to the placebo group, based on visual analog scale scores.Takanari 2015

In another study in cancer patients with increased HHV-6 levels during the first course of chemotherapy, AHCC decreased HHV-6 at the end of the second course of chemotherapy and increased quality of life in female patients. Given the fluctuations in HHV-6 levels, these results suggest that AHCC may contribute to immune-enhancing effects, resulting in inhibition of reactivation of HHV-6. The immunologically activating effects may also explain the inhibition of leukopenia, neutropenia, thrombocytopenia, and impairment of liver function that were observed.Ito 2014

In a study in healthy adults, an AHCC dosage of 3 g/day for 3 weeks was given to determine its effectiveness in improving immune responses to influenza vaccination. Data showed sustained levels of B cells, natural killer cells, CD4 T cells, and T cells, as well as increased antibody titers against influenza B. The AHCC group showed a trend for increased natural killer T cell fold change as well as an increase in $CD8^+$ cytotoxic T cell fold change. More patients in the AHCC group showed improvements in their influenza B

antibody titers in terms of seroprotection and seroconversion. The study results suggest that AHCC improves cell-mediated immune response after influenza vaccination.Roman 2013

Infection

In vitro and animal data

Oral administration of AHCC to food-deprived mice infected with Klebsiella pneumonia promoted clearance of the bacteria and resulted in reduced bacterial load. AHCC also enhanced early immune response by increasing levels of proinflammatory cytokines (ie, IL-12, TNF-alpha, IL-6) and chemokines (MCP-1) that promote clearance and reduction of a variety of pathogens.Aviles 2008 In other studies in mice maintained in the hindlimb-unloading model, AHCC decreased mortality, prolonged time to death, and increased clearance of K. pneumonia infection in mice.Aviles 2003, Aviles 2004 A similar study in mice reported that AHCC helped to restore immunity after trauma, infection, and food deprivation.Aviles 2006

In a study of mice infected with influenza virus, AHCC increased survival, enhanced natural killer cell activity in the lung and spleen, and rapidly cleared the primary influenza infection or virus from the lungs.Pescatore 2008 The compound works in a dose-dependent manner against acute influenza infection.Nogusa 2009

AHCC may be useful as a prophylactic drug in managing patients with opportunistic infections. The survival period for mice with cyclophosphamide-induced leukopenia was prolonged after oral or intraperitoneal administration of AHCC 50 or 1,000 mg/kg/day prior to Candida albicans infection. The kidneys of infected mice also had decreased viable counts of C. albicans. Oral administration of AHCC protected mice from a lethal Pseudomonas aeruginosa infection, and intraperitoneal administration protected mice from methicillin-resistant Staphylococcus aureus infection.Ikeda 2003, Ishibashi 2000

AHCC administered to aged mice with West Nile encephalitis attenuated viremia levels but resulted in no difference in mortality rate.Wang 2009

In a cecal ligation and puncture model of peritonitis, mice were pretreated with 1 g/kg of AHCC or water by gavage for 10 days before undergoing cecal ligation and puncture, then daily following infection. In those pretreated with AHCC, cortisol levels decreased over time in plasma and peritoneal samples, which indicates that AHCC diminishes local and systemic cortisol concentrations. AHCC also seemed to restrain systemic, but not local norepinephrine concentrations; this may prove to be a possible preventative mechanism in avoiding overstimulation of the generalized inflammatory response that leads to systemic inflammatory response syndrome. A relative decrease in bacterial load and increase in neutrophil infiltration indicated an early trend toward promoting clearance of local infection.Love 2013

Clinical data

Clinical trials conducted in Bangkok report that HIV patients treated with AHCC demonstrated increased or maintained T-cell counts and increased natural killer cell activity; however, the details of these studies are lacking.Kenner 2001

AHCC 3 g/day was evaluated for 12 months in 20 HIV-positive men. The results of the study were as follows: Natural killer cell activity was enhanced during the first month and peaked at the third month and remained consistent during the trial; absolute $CD4^+$ cell counts showed a marked increase in 14 of 20 patients during the first month, which remained consistent; percentage of $CD4^+$ cells showed no change; absolute CD8 cell counts increased in 12 of 20 patients; and $CD4^+/CD8^+$ ratio showed no change.Ghoneum 1994

In a study in healthy older individuals receiving AHCC, a dose of three 500 mg capsules orally twice daily for 60 days produced enhanced $CD4^+$ and $CD8^+$ T-cell immune responses due to increased production of cytokines (IFN-gamma alone, TNF-alpha alone, or both) from T cells, which suggests a potential role for AHCC in improving host defense against infections and malignancy in humans by enhancing T-cell immune function. Effects of AHCC may last several weeks after AHCC discontinuation, based on increased levels of $CD4^+$ 30 days after discontinuation.Yin 2010

Inflammatory bowel disease

Animal data

In rat colitis models, the anti-inflammatory effect of AHCC was comparable with sulfasalazine 200 mg/kg. AHCC reduced colonic inflammation and improved body weight, food intake, extension of necrosis, colonic weight, colonic weight-to-length ratio, expression of proinflammatory cytokines and chemokines (IL-1b, IL-1 receptor antagonist, TNF, and monocyte chemoattractant protein-1), and mucosal barrier defense (mucins 2 to 4 and trefoil factor 3). When assessing AHCC's effect on colonic microflora by studying the bacteria profile in feces, rats treated with AHCC had higher aerobic and lactic acid bacteria counts, and higher bifidobacteria counts, indicating potential use as a prebiotic.Daddaoua 2007

A study in mice evaluated the anti-inflammatory effects of a 75 mg/day dose of AHCC on the $CD4^+CD62L^+$ T-cell transfer model of colitis. There was a positive response to AHCC, as evidenced by a lower disease activity index, colonic myeloperoxidase and alkaline phosphatase activities, and diminished ex vivo production of IL-6, IL-17, and IL-10 by mesenteric lymph node cells. There was a lower sensitivity of alkaline phosphatase activities to levamisole in vitro. AHCC also produced increased colonic expression of a variety of inflammatory markers, in particular TNF-alpha and IL-1beta. Furthermore, it normalized the mRNA level increased by colitis and decreased cyclooxygenase 2. AHCC also demonstrated inhibition of STAT4 phosphorylation in splenic $CD4^+$ cells. There were no changes in mRNA levels of IFN-gamma, TNF-alpha, or IL-1beta in spleen cells, suggesting that AHCC exerts systemic immunomodulatory effects, which possibly reduces the number of IFN-gamma–producing Th1 cells. A disruption in efficient control of mucosa-invading microorganisms may evoke an inflammatory response, therefore

supporting the potential anti-inflammatory role of AHCC in IBD. AHCC may also limit inflammation of the colon by enhancing mucosal barrier function.Mascaraque 2014

Liver dysfunction or injury/hepatoprotection

Excess nitric oxide production may be involved with liver injury. AHCC may decrease inducible nitric oxide synthase (iNOS) by reducing mRNA stabilization, rather than by inhibiting its synthesis.Matsui 2007, Matsui 2008

In vitro data

In primary cultured hepatocytes, simultaneous administration of AHCC-sugar fraction (AHCC-sf) 1 to 8 mg/mL with IL-1beta decreased nitric oxide production. Levels of iNOS protein and iNOS mRNA were also decreased, which suggests AHCC-sf inhibits the induction of iNOS gene expression at a transcriptional and/or posttranscriptional step in proinflammatory cytokine-stimulated hepatocytes. These results suggest AHCC has liver-protectant effects.Matsui 2011

Clinical data

In patients with liver injury due to excessive alcohol ingestion, AHCC supplementation at dosages of 1 g/day (three 167 mg capsules 30 minutes before breakfast and dinner) and 3 g/day (three 500 mg capsules 30 minutes before breakfast and dinner) for 12 weeks improved ALT levels, decreased TNF-alpha and IL-1beta, and elevated adiponectin without any adverse effects. The improvement in liver enzyme levels, decrease in proinflammatory cytokines, and elevation of anti-inflammatory cytokines indicate that AHCC is beneficial in liver injury. No adverse events occurred in either group.Kim 2014

In another study, patients with chronic hepatitis C received AHCC 2 g 3 times daily for 24 weeks, which demonstrated reductions in HCV RNA levels in genotype-3 patients and control of ALT levels in all patients.Thaiudom 2010

Dosing

AHCC is primarily available as a capsule. Manufacturer dosing guidelines recommend two 500 mg capsules orally 3 times a day on an empty stomach, or 2 capsules orally daily for general well-being. In one study, a dose of 3 g/day for 4 weeks led to an increase in specific innate immunity.Terakawa 2008

Cancer

1 g of AHCC taken orally after each meal was used in a clinical trial to improve bone marrow suppression and reduce adverse effects of chemotherapy (ie, neutrophil-related adverse events, lipid abnormalities) in breast cancer patients.Hangai 2013

AHCC 6 g/day for 8 weeks has been used to improve gemcitabine-induced adverse events in patients with unresectable pancreas ductal adenocarcinoma receiving gemcitabine.Yanagimoto 2016

AHCC 3 g/day orally during a course of chemotherapy has been used for its effects on chemotherapy-induced adverse effects (eg, fatigue) to improve quality of life in patients with advanced cancer.Ito 2014

Two 500 mg capsules of AHCC orally 3 times daily throughout 6 cycles of chemotherapy has been used in a study of epithelial ovarian cancer or peritoneal cancer patients to decrease adverse effects associated with platinum-based chemotherapy (eg, nausea and vomiting).Suknikhom 2017

In a study of head and neck cancer patients, 3 g of dried AHCC extract has been administered every morning 3 days prior to chemotherapy to reduce chemotherapy-associated adverse effects (ie, GI-related) and increase sense of well-being, thereby helping to improve tolerance of further chemotherapy cycles.Parida 2011

Immune suppression

4 capsules (250 mg/capsule) daily for 4 weeks has been used to maintain immune competence against seasonal changes.Takanari 2015

AHCC 3 g/day for 3 weeks has been used to improve immune response to influenza vaccination.Roman 2013

Infection

Three 500 mg capsules of AHCC orally twice daily for 60 days was administered in healthy individuals to evaluate its potential role in improving host defense against infections and malignancy in humans via enhancement of T-cell immune function.Yin 2010

Liver dysfunction or injury

Three 500 mg capsules of AHCC orally 30 minutes before breakfast and dinner for 12 weeks has been used in a study evaluating the hepatoprotective effects of AHCC in patients with liver injury due to excessive alcohol ingestion. In the same study, another group was given three 167 mg capsules orally 30 minutes before breakfast and dinner for 12 weeks.Kim 2014

AHCC 2 g 3 times daily for 24 weeks has been used in a study for the management of chronic hepatitis C.Thaiudom 2010

Pregnancy / Lactation

Information regarding safety and efficacy in pregnancy and lactation is lacking.

Interactions

CYP induction metabolism assays indicate that AHCC induces CYP2D6 by a similar mechanism as doxorubicin; however, one study did not demonstrate interference of AHCC with tamoxifen activity in mice but did show a decrease in letrozole activity when given in combination with AHCC.Mathew 2017 Data suggest that AHCC is safe to administer with most other chemotherapy agents not metabolized by CYP2D6.Ito 2014 Data also show that AHCC potentially induces aromatase enzyme activity when given alone.Mathew 2017 Concomitant use with aromatase inhibitors is not recommended until further studies have been conducted.

Adverse Reactions

Historically, the safety profile of AHCC has been well established. A phase 1 trial documented mild GI complaints, including nausea, diarrhea, and bloating. Some patients reported headache, fatigue, and foot cramps with the liquid form of AHCC.Spierings 2007 In one study, patients complained of nausea and intolerance.Fujii 2011 One patient in another study experienced diarrhea in the first 2 weeks of AHCC use, which subsided without treatment.Thaiudom 2010

Toxicology

Avoid use in patients who are hypersensitive to any of the components of AHCC or to basidiomycete mushrooms. In a phase 1 trial, AHCC 9 g/day for 14 days resulted in minimal adverse reactions and was well tolerated by most healthy subjects.Spierings 2007 In rats, the median lethal dose of AHCC was 8,490 mg/kg in males and 9,849 mg/kg in females. Intraperitoneally, the minimal lethal dose of AHCC was lower in male than in female rats (7,430 mg/kg and 8,340 mg/kg, respectively).Hirose 2007

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